



Prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis

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ARTICLE INFO

ABSTRACT

Article type

Review article

Article history

Received: 21 Jan 2014

Revised: 31 Jan 2014

Accepted: 8 Apr 2014

Keywords

Pancreatitis
Pharmacologic agent
Endoscopic Retrograde
Cholangiopancreatography
(ERCP)

Pancreatitis is the most common and important complication of endoscopic retrograde cholangiopancreatography (ERCP). Several risk factors play a role in the formation and progression of pancreatitis. These risk factors may be related to the patient, procedure or operator. All of these risk factors should be considered and should be lowered as far as possible with attention to pathogenesis of the development of post-ERCP pancreatitis. The pathogenesis include sphincter spasm, infection, contrast toxicity and pancreatic secretion that induce the activation of proteolytic enzymes and inflammatory processes. Some methods and pharmacologic agents assessed for the prevention of pathway in the pathogenesis to decrease post-ERCP pancreatitis.

Please cite this paper as:

Hoseini SM, Esmaealzadeh A, Salari M, Dadpour B, Yekta Roudi K, Yekta Roudi M, Javid Arabshahi Z. Prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. *Rev Clin Med.* 2014;1(3):149-153.

Introduction

About 75 percent of patients after endoscopic retrograde echolangiopancreatography (ERCP) may have elevation of serum amylase, but acute clinical pancreatitis (defined as a clinical syndrome of abdominal

pain and hyperamylasemia) is less common. However, acute pancreatitis is the most important complication of ERCP and the attention should be paid to prevent its morbidity and mortality (1).

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Mechanism for post-ERCP pancreatitis (PEP)

The exact mechanism for PEP is unknown. A trigger event needs to turn on the inflammatory process as following: thermal injury from sphincterotomy, mechanical obstruction of the outflow of the pancreatic secretions, papillary edema from attempted multiple cannulations, injury from guidewire, chemical injury of the contrast, microbiological injury due to introduction of duodenal flora into the pancreas etc (2).

Risk Factors for post-ERCP pancreatitis

It is important to identify cases at high risk of pancreatitis in who the complications can be prevented by prophylactic methods such as pancreatic stenting or pharmacological prophylaxis. Assessment of both patient- and procedure-related factors is necessary to detect the high-risk cases (Table 1) (3).

Definition of post-ERCP pancreatitis

There need to be at least two of the following criteria to diagnose PEP:

1. Epigastric pain with radiation to the back,
2. Elevation of amylase and/or lipase at least 3 times higher than normal,
3. Radiological imaging that suggests pancreatitis

Amylase and lipase may have an elevation despite the patients do not have any symptoms. Radiological imaging is helpful when the diagnosis is difficult (4).

Methods and pharmacologic prevention of post-ERCP pancreatitis

A. If the following techniques use, the risk of post-ERCP pancreatitis will decrease:

1. Endoscopic techniques
2. Cannulation
3. Electrocautery
4. Pancreatic stenting

B. Drugs that may prevent post-ERCP including nonsteroidal anti-inflammatory drugs (NSAIDs), steroidal anti-inflammatory agents, inhibitors of pancreatic secretion, agents that reduce sphincter tone, inhibitors of protease activation, antioxidants, antimicrobial agents and antimetabolites (1).

Some of the drugs that tested in different trials are described below:

Pharmacological prevention for post-ERCP pancreatitis**1- NSAIDs**

NSAIDs (diclofenac or indomethacin) are the most common drugs that are using for the prevention of post-ERCP pancreatitis (5).

The European Society of Gastrointestinal Endoscopy recommends routine rectal administration of 100 mg diclofenac or indomethacin for the prevention of post-ERCP pancreatitis (6).

2- Glyceryl trinitrate

Glyceryl trinitrate reduces sphincter of Oddi pressure and may use to prevent post-ERCP pancreatitis. Manuel Moretó in his study assessed whether transdermal glyceryl

Table 1. Risk Factors for post-ERCP pancreatitis

Patient-related factors	Procedure-related factors	Operator-related factors
Sex (Female)	Precut sphincterotomy	Experience of operator
Oddi sphincter dysfunction	Pancreatic duct injection	
History of Previous Pancreatitis	Balloon dilation	
Chronic pancreatitis absent	Pancreatic sphincterotomy	
age <60 years	Difficult cannulation	
Normal bilirubin	Minor papilla sphincterotomy	
	Pain during ERCP	
	Ampullectomy	

trinitrate could be effective in the prevention of post-ERCP pancreatitis or not. The results of his study showed that transdermal glyceryl trinitrate patch significantly reduced post-ERCP pancreatitis (5).

3- Nifedipine

Calcium channel inhibitors can prevent the development of experimental pancreatitis. Nifedipine is a calcium channel blocker drug and its effect is reducing the sphincter spasm. Part performed a randomized, placebo-controlled trial to determine whether the calcium channel blocker, nifedipine, prevented post-ERCP pancreatitis or not. Nifedipine or placebo was administered before and within 6 hours after ERCP. This study could not show the significant effect of nifedipine in the prophylaxis of post-ERCP pancreatitis (6).

4-Antibiotics

Infections following ERCP can activate the proteolytic enzymes and can lead to pancreatitis. Now there is a question that if antibiotics can use in the prevention of post-ERCP pancreatitis. One prospective randomized controlled trial showed that the ceftazidime administration before ERCP significantly decreased the incidence of post-ERCP pancreatitis compared to the control group that did not receive antibiotic (7). The quality of the study is questionable because the control group did not receive any antibiotic (2).

5- Risperidone

Ulinastatin inhibited systemic inflammatory responses and may be beneficial for prevention post-ERCP pancreatitis. Tsujino assessed the effect of risperidone (a selective serotonin 2A antagonist) combined with ulinastatin for the prevention of PEP in high-risk patients.

In a multicenter, randomized, controlled

trial, patients were randomly received the administration of ulinastatin with or without risperidone.

The incidence of PEP was not significantly different between two groups, but pancreatic enzymes level were significantly lower in the risperidone + ulinastatin group as compared with ulinastatin alone (9).

6- Indomethacin

Indometacin is a nonsteroidal antiinflammatory drug that is used for prevention of post-ERCP pancreatitis.

Joseph Elmunzer in a multicenter, randomized, placebo-controlled, double-blind clinical trial assigned high-risk patients for post-ERCP pancreatitis to receive a single dose of indomethacin or placebo immediately after ERCP. Among patients at high risk for post-ERCP pancreatitis, rectal indomethacin significantly reduced the incidence of the post-ERCP pancreatitis (10).

Yaghoobi also assigned one meta-analysis to assessed rectal indomethacin for the prevention of post-ERCP pancreatitis. This meta-analysis showed that the rate of pancreatitis was significantly lower using indomethacin as compared with placebo (11).

7-Corticosteroid

Corticosteroids are anti-inflammatory drugs that may be able to decrease the risk of post-ERCP pancreatitis.

In a prospective randomized controlled multicentre study, administration of prednisone did not reduce the incidence of pancreatitis compared to placebo (12).

8- N-acetyl cysteine (NAC)

N-acetyl Cysteine can reduce inflammation and may be useful in post-ERCP pancreatitis. Pezhman Alavi Nejad evaluated the efficacy of N-acetyl cysteine for the prevention of post-ERCP. He assigned a prospective double blind randomized study. There were

significant reduction in the prevalence of acute pancreatitis between two groups. This study showed that NAC could be used for the prevention of post-ERCP pancreatitis (13).

9 -Aprepitant

Aprepitant is a drug of neurokinin-1 receptor antagonist classification. Upendra Shah assessed the efficacy of aprepitant in the prevention of post-ERCP pancreatitis in high-risk patients. A randomized, double blind, placebo controlled trial assigned. Patients received either placebo or oral aprepitant. Aprepitant could not decrease the incidence of post-ERCP pancreatitis as against placebo (14).

Pancreatic stents

Abhishek Choudhary assessed a meta-analysis and determined the effect of pancreatic stents for the prevention of post-ERCP pancreatitis. This meta-analysis of the RCTs showed that pancreatic stent placement reduced the incidence pancreatitis and hyperamylasemia (14).

Conclusion

Considering the fact that pancreatitis is the most important complication of the ERCP, we should pay more attention to the prevention methods of post-ERCP pancreatitis. Pancreatic stents are useful for this aim. From the pharmacologic agents, glyceryl trinitrate, indometacin and N-acetyl cysteine could significantly decrease the incidence of post-ERCP pancreatitis. Other drug that were assessed in this review article such as nifedipine, risperidone, corticosteroids and aprepitant did not show significant effect in the prevention of post-ERCP pancreatitis.

Acknowledgement

We would like to thank Clinical Research Development Center of Ghaem Hospital for

their assistant in this manuscript. This study was supported by a grant from the Vice Chancellor for Research of the Mashhad University of Medical Sciences for the research project as a medical student thesis.

Conflict of Interest

The authors declare no conflict of interest.

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